IN THE CLAIMS

1. (Currently Amended) A computer-implemented method of predicting a pharmacokinetic property of a target compound in an anatomical segment of a target mammalian system from a pharmacokinetic property of a test compound ~~in an anatomical segment of a data source system~~, said computer comprising as operably linked components:

~~(a)~~ an input/output system,

~~(b) a simulation engine,~~ and

~~(c)~~ a stored physiologic pharmacokinetic simulation model of said mammalian system, said simulation model comprising:

differential equations for calculating a change in one or more physiological parameters of said target mammalian system and the movement and disposition of said target compound in said mammalian system as a function of time, using input data for said differential equations comprising a pharmacokinetic property of the test compound ~~in the anatomical segment of said data source system~~; and

a logic function module having control statement rules for initiating said physiologic pharmacokinetic simulation model of said mammalian system function,

wherein said simulation model generates estimated values for a selected pharmacokinetic property of said target compound when supplied with input values

corresponding to said selected pharmacokinetic property of said test compound ~~in a portion of said data source system~~

said method comprising:

(a) entering into said input/output system input data comprising the pharmacokinetic property of said test compound ~~in the segment of said data source system~~; and

(b) applying ~~said simulation engine and~~ said simulation model~~, and initiating said estimation function~~ to predict said pharmacokinetic property of said target compound in a segment of said target mammalian system,

wherein the simulation model comprises a selected adjustment parameter and wherein the selected adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selected adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selected adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selected adjustment parameter in the simulation model with the new value selected in step (iv).

2. (Currently Amended) A computer-implemented method of predicting a pharmacokinetic property of a compound in a first anatomical segment of a mammalian system of interest from a pharmacokinetic property of said compound in a second anatomical segment of said mammalian system of interest, said method comprising:

providing a computer having as operably linked computer-implemented components an input/output system, a simulation engine, and a physiologic pharmacokinetic simulation model of at least first and second anatomical segments of said mammalian system of interest, said simulation model comprising (i) ~~differential~~ equations for calculating the change in one or more physiological parameters of said first and second segments and the movement and disposition of said compound in said first and second segments as a function of time, and (ii) a logic function module having a regional correlation parameter estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property ~~comprising an absorption parameter~~ of said compound in said first segment when supplied with an input value corresponding to said selected pharmacokinetic property of said compound in said second segment and with a regional correlation coefficient for said selected pharmacokinetic parameter of said first and second segments;

entering into said input/output system input data comprising a pharmacokinetic property of said compound in said second segment; and

applying said simulation engine and said simulation model, and initiating said estimation function to predict said pharmacokinetic property of said compound in said first segment of said mammalian system of interest,

wherein the regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the regional correlation coefficient;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient in the logic function module with the new value selected in step (iv).

3. (Original) The method of claim 2, wherein said regional correlation estimation function comprises a function/transformation algorithm.

4. (Original) The method of claim 3, wherein said function/transformation algorithm is selected from the group consisting of a polynomial, exponential, and logarithm.

5. (Original) The method of claim 2, wherein said regional correlation coefficient comprises a best fit value that transforms said input data comprising said pharmacokinetic property of said compound in said second segment to an estimated pharmacokinetic property of said compound in said first segment.

6. (Original) The method of claim 2, wherein said pharmacokinetic property is selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

7. (Original) The method of claim 2, wherein said pharmacokinetic parameter is selected from the group consisting of permeability, solubility, dissolution rate and transport mechanism.

8. (Currently Amended) The method of claim 2, wherein said ~~differential~~ equations are selected from the group consisting of equations for fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption.

9. (Original) The method of claim 2, which further comprises reversibly storing said estimated value for said pharmacokinetic parameter of said compound in said first segment in a computer-implemented database.

10. (Original) The method of claim 2, which further comprises reversibly storing in a computer-implemented database an output value corresponding to said pharmacokinetic property of said compound in a segment of said mammalian system that is generated by applying said simulation engine and said simulation model.

11. (Original) The method of claim 2, wherein said mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

12. (Original) The method of claim 2, wherein said mammalian system of interest is human.

13. (Original) The method of claim 2, wherein said input data comprises in vitro data.

14. (Original) The method of claim 13, wherein said in vitro data is derived from testing of said compound in an assay that generates data selected from the group consisting of cell, tissue, physicochemical, structure-activity relationship (SAR) SAR, and quantitative structure-activity relationship (QSAR) QSAR data.

15. (Original) The method of claim 2, wherein said computer is a computer system having a data processor, a memory and a display.

16. (Original) The method of claim 2, wherein said computer is a standalone computer having a data processor, a memory and a display.

17. (Original) The method of claim 2, wherein said computer-implemented components comprise computer readable program code.

18. (Original) The method of claim 17, wherein said computer readable program code is embodied in a computer readable medium.

19. (Currently Amended) A computer-implemented method of simulating one or more parameters of absorption of a compound in a mammalian system of interest using regional correlation parameter estimation, said method comprising:

providing a computer having as operably linked computer-implemented components an input/output system~~, a simulation engine,~~ and a physiologic pharmacokinetic simulation model of at least two segments of mammalian system of interest having one or more absorption barriers to a compound based on the selected route of administration, said simulation model comprising (i) differential equations for calculating one or more parameters of absorption of said compound in said segments as a function of time and (ii) a logic function module having a regional correlation parameter estimation function and a control statement for initiating said estimation function, said estimation function when initiated being capable of generating an estimated value for a parameter of absorption of said compound in a first segment of said mammalian system utilizing an input value for said parameter of absorption of said compound in a second segment of said mammalian system and a regional correlation coefficient;

entering through said input/output system input data comprising a parameter of absorption for said compound in said second segment; and

applying said simulation engine and said simulation model, and initiating said estimation function to simulate one or more parameters of absorption of said compound in said first segment of said mammalian system of interest~~,~~

wherein the regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the regional correlation coefficient;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient in the logic function module with the new value selected in step (iv).

20. (Currently Amended) A method of simulating a pharmacokinetic parameter of a compound in a mammalian system of interest, said method comprising:

providing a computer having as operably linked computer-implemented components an input/output system~~, a simulation engine,~~ and a physiologic pharmacokinetic simulation model of one or more segments of a selected mammalian system having one or more physiological barriers to absorption of said compound based on a selected route of administration, said simulation model comprising: (i) differential equations for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system; (ii) a regional correlation parameter estimation function for one or more of permeability, solubility, dissolution rate and transport mechanism; (iii) initial parameter values for said

differential equations corresponding to physiological parameters and ~~one or more regional correlation parameters~~ regional correlation coefficient for one or more segments of said mammalian system; and (iv) control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammalian system;

entering through said input/output system input data comprising dose, permeability and solubility data for said compound for one or more segments of said mammalian system; and

applying ~~said simulation engine and~~ said simulation model to simulate one or more pharmacokinetic parameters of said compound relative to one or more segments of said mammalian system,

wherein the regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the regional correlation coefficient of the simulation model;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient in the simulation model with the new value selected in step (iv)

21. (Original) The method of claim 20, wherein said pharmacokinetic parameters of said compound relative to one or more segments of said mammalian system are selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

22. (Currently Amended) A method of simulating absorption of a compound in a mammal utilizing a pharmacokinetic simulation tool (PK tool), said method comprising:

providing a computer-implemented PK tool comprising an input/output system~~, a simulation engine,~~ and a simulation model of one or more segments of a mammalian system of interest having one or more physiological barriers to absorption based on the selected route of administration, said simulation model comprising as operably linked components: (i) differential equations for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammal system; (ii) initial parameter values for said differential equations corresponding to physiological parameters and selectively optimized adjustment parameters, and ~~optionally~~ regional correlation parameters, for one or more segments of said mammalian~~mammal~~ system; and (iii) control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammal system;

entering into said input/output system input data comprising dose, permeability and solubility data for said compound for one or more of said segments of said mammalian~~mammal~~ system; and

applying ~~said simulation engine and~~ said simulation model to simulate absorption of said compound in said mammalian~~mammal~~ system,

wherein the selectively optimized adjustment parameters comprise values obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameters;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting new values for the selectively optimized adjustment parameters such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the values of the selectively optimized adjustment parameters in the simulation model with the new values selected in step (iv); and

wherein the regional correlation parameters comprise values obtained by:

(i) assigning an initial value to the regional correlation parameters;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the model and running the model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting new values for the regional correlation parameters such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the values for the regional correlation parameters in the simulation model with the new values selected in step (iv).

23. (Currently Amended) A computer-implemented method of predicting a pharmacokinetic property of a compound in a mammalian system of interest, said method comprising:

providing a computer comprising as operably linked computer-implemented components an input/output system, a simulation engine, and a physiologic pharmacokinetic simulation model of two or more segments of a mammalian system of interest, wherein said simulation model comprises ~~differential~~ equations for calculating as a function of time the change in (i) a physiological parameter of one or more of said segments and (ii) a pharmacokinetic property ~~comprising an absorption parameter~~ of a compound ~~relative to a selected route of administration, barrier to absorption and sampling site of one or more of said segments~~, and wherein one or more of said ~~differential~~ equations is modified by a selectively optimized adjustment parameter;

entering through said input/output system input data comprising dose, permeability and solubility data for said compound for one or more of said segments of said mammalian~~mammal~~ system; and

applying said simulation engine and said simulation model to predict a pharmacokinetic property of said compound in one or more segments of said mammalian~~mammal~~ system of interest,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively optimized adjustment parameter in the simulation model with the new value selected in step (iv).

24. (Original) The method of claim 23, wherein said computer is a computer system having a data processor, a memory and a display.

25. (Original) The method of claim 23 wherein said computer is a standalone computer having a data processor, a memory and a display.

26. (Original) The method of claim 23, wherein said computer-implemented components comprise computer readable program code.

27. (Original) The method of claim 26, wherein said computer readable program code is embodied in a computer readable medium.

28. (Original) The method of claim 26, wherein said computer readable program code is embodied in said memory.

29. (Original) The method of claim 23, wherein said input/output system comprises a user interface.

30. (Currently Amended) The method of claim 23, wherein said simulation engine comprises ~~a differential~~ an equation solver.

31. (Currently Amended) The method of claim 23, wherein said ~~differential~~ equations are for fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption.

32. (Original) The method of claim 23, wherein said pharmacokinetic property is selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

33. (Currently Amended) The method of claim 23, wherein said pharmacokinetic property ~~absorption parameter~~ is selected from the group consisting of concentration, permeability, solubility, dissolution rate, transport mechanism, and formulation release rate.

34. (Original) The method of claim 23, wherein said physiological parameter is selected from the group consisting of pH, initial fluid volume, surface area, transit time, fluid volume transfer rate, and fluid absorption.

35. (Original) The method of claim 23, wherein said mammalian system of interest is human.

36. (Original) The method of claim 23, wherein said mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

37. (Original) The method of claim 23, wherein said simulation model comprises one or more control statement rules.

38. (Currently Amended) The method of claim 37, wherein said control statement rules are for controlling simulation of one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said ~~mammal~~ mammalian system of interest.

39. (Original) The method of claim 23, wherein said input data further comprises data selected from the group consisting of dissolution rate, transport mechanism and formulation release rate.

40. (Original) The method of claim 23, wherein said equations comprise one or more input variables corresponding to said input data for calculating as one or more output variables said change in said physiological parameter.

41. (Currently Amended) The method of claim 23, wherein said equations comprise one or more input variables corresponding to said input data for calculating as one or more output variables said change in said pharmacokinetic property ~~absorption parameter~~.

42. (Original) The method of claim 23, wherein said selectively optimized adjustment parameter correlates said input data to output data comprising said pharmacokinetic property of said compound.

43. (Original) The method of claim 42, wherein said input data comprises in vitro data and said selectively optimized adjustment parameter comprises a best fit value obtained by (i) assigning an initial value to a selected adjustment parameter of said simulation model, (ii) fitting a combination of in vitro data and in vivo data for different compounds of a compound test set with said simulation model, (iii) selecting a best fit value for selected adjustment parameter that, when assigned as an initial value to said selected adjustment parameter, permits said simulation model to predict said pharmacokinetic property of said compound when said input data comprises said in vitro data, and (iv) assigning said best fit value to said selected adjustment parameter so as to generate said selectively optimized adjustment parameter.

44. (Original) The method of claim 43, wherein said in vitro data is obtained from testing of said compound in one or more assays that generate data selected from the group consisting of cell, tissue, structure-activity relationship (SAR), and quantitative structure-activity relationship (QSAR) data.

45. (Original) The method of claim 43, wherein said different compounds of a compound test set comprise compounds having diverse pharmacokinetic properties.

46. (Original) The method of claim 42, wherein said input data comprises in vivo data from a first species of mammal and said mammalian system of interest corresponds to a second species of mammal, and wherein said selectively optimized adjustment parameter comprises a best fit value obtained by (i) assigning an initial value to a selected adjustment parameter of said simulation model, (ii) fitting a combination of in vivo data with said simulation model, said combination of in vivo data being derived from testing of different compounds of a compound test set in said first species of mammal and said second species of mammal, (iii) selecting a best fit value for selected adjustment parameter that, when assigned as an initial value to said selected adjustment parameter, permits said simulation model to predict said pharmacokinetic property of said compound when said input data comprises said in vitro data from said first species of mammal, and (iv) assigning said best fit value to said selected adjustment parameter so as to generate said selectively optimized adjustment parameter.

47. (Original) The method of claim 46, wherein said different compounds of a compound test set comprise compounds having diverse pharmacokinetic properties.

48. (Original) The method of claim 23, wherein said selectively optimized adjustment parameter is for one or more of fluid absorption, flux, permeability, transport mechanism, transfer rate, and segment surface area.

49. (Original) The method of claim 22 or 23, which further comprise reversibly storing in a computer-implemented database data corresponding to a predicted pharmacokinetic property of said compound.

50. (Currently Amended) The method of claim 23, wherein said physiologic pharmacokinetic simulation model ~~module~~ comprises at least two of said anatomical segments and a logic function model comprising a regional correlation estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property of said compound in a first anatomical segment when supplied with an input value corresponding to said selected pharmacokinetic property in a second anatomical segment and with a regional correlation coefficient for said selected pharmacokinetic property of said first and second anatomical segments.

51. (Original) The method of claim 50, wherein said regional correlation estimation function comprises a function/transformation algorithm.

52. (Original) The method of claim 51, wherein said function/transformation algorithm is selected from the group consisting of a polynomial, exponential, and logarithm.

53. (Original) The method of claim 50, wherein said regional correlation coefficient comprises a best fit value that transforms said input data comprising said pharmacokinetic property of said compound in said second segment to an estimated pharmacokinetic property of said compound in said first segment.

54-79. Cancel.

80. (Currently Amended) A computer system configured to predict a pharmacokinetic property of a target compound in a target anatomical segment of a target mammalian system from a pharmacokinetic property of a test compound ~~in an anatomical segment of a data source system~~, said computer comprising as operably linked components:

~~(a)~~ an input/output system,

~~(b) a simulation engine,~~ and

~~(c)~~ a stored physiologic pharmacokinetic simulation model of said target mammalian system, said simulation model comprising:

(i) differential equations for calculating a change in one or more physiological parameters of said target mammalian system and the movement and disposition of said target compound in said target mammalian system as a function of time, using input data for said differential equations comprising the pharmacokinetic property of the test compound in the anatomical segment of said data source system; and

(ii) boundary condition parameter values for said differential equations corresponding to parameters of said target mammalian system, and

(iii) a logic function module having control statement rules for initiating said physiologic pharmacokinetic simulation model of said mammalian system function, wherein the simulation model comprises a selected adjustment parameter and wherein the selected adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selected adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selected adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selected adjustment parameter in the simulation model with the new value selected in step (iv).

81. (Currently Amended) The computer system of claim 80 wherein said computer, using the simulation model, generates estimated values for a selected pharmacokinetic property of said target compound when supplied with input values corresponding to said selected pharmacokinetic property of said test compound ~~in a portion of said data source system~~ by the method comprising:

(a) entering into said input/output system input data comprising a pharmacokinetic property of said test compound in a segment of said data source system; and

(b) applying ~~said simulation engine and~~ said simulation model~~,~~ and invoking said simulation ~~engine~~ model for predicting said pharmacokinetic property of said target compound in a segment of said target mammalian system.

82. (Currently Amended) A computer system for simulating absorption of a compound in a mammal, said system having as computer-implemented components an

input/output system~~, simulation engine,~~ and simulation model of one or more segments of a selected mammalian system having one or more physiological barriers to absorption based on a selected route of administration, said simulation model comprising as operably linked components:

(i) differential equations for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system; (ii) initial parameter values for said differential equations corresponding to physiological parameters and selectively optimized adjustment parameters, and ~~optionally~~ regional correlation parameters, for one or more segments of said mammalian system; and (iii) control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammalian system;

said input/output system~~, said simulation engine,~~ and said simulation model being capable of working together to carry out the steps of:

(a) receiving as input data through said input/output system, dose, permeability and solubility data for said compound for one or more segments of said mammalian system; and

(b) applying ~~said simulation engine~~ and said simulation model to simulate absorption of said compound relative to one or more segments of said mammalian system,

wherein the selectively optimized adjustment parameters comprise values obtained by:

(i) assigning initial values to the selectively optimized adjustment parameters;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting new values for the selectively optimized adjustment parameters such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the values of the selectively optimized adjustment parameters in the simulation model with the new values selected in step (iv); and

wherein the regional correlation parameters comprise values obtained by:

(i) assigning initial values to the regional correlation parameters of the simulation model;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting new values for the regional correlation parameters such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the values for the regional correlation parameters in the simulation model with the new values selected in step (iv).

83. (Currently Amended) A computer system for simulating a pharmacokinetic property of a compound in a mammalian system of interest, said computer system comprising as operably linked computer-implemented components an input/output system~~, a simulation engine,~~ and a physiologic pharmacokinetic simulation model of one or more anatomical segments of said mammalian system of interest, said simulation model ~~comprising differential~~ equations for ~~calculating~~ predicting as a function of time the change in (i) a physiological parameter of one or more of said segments and (ii) a pharmacokinetic property ~~comprising an absorption parameter~~ of a compound relative to a selected route of administration~~, barrier to absorption and sampling site of one or more of said segments,~~ wherein one or more of said ~~differential~~ equations ~~is~~ are modified by a selectively optimized adjustment parameter;

said input/output system~~, said simulation engine,~~ and said physiologic pharmacokinetic simulation model being capable of working together to carry out the steps of:

(a) receiving through said computer readable input/output system input data comprising dose, permeability and solubility data for said compound for one or more segments of said mammalian system of interest; and

(b) applying ~~said simulation engine and~~ said physiologic pharmacokinetic simulation model to simulate a pharmacokinetic property of said compound relative to one or more segments of said mammalian system of interest,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively optimized adjustment parameter in the model with the new value selected in step (iv).

84. (Currently Amended) The computer system of claim 83, wherein said ~~differential~~ equations are for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system.

85. (Currently Amended) The computer system of claim 83, wherein said ~~differential~~ equations comprise initial parameter values corresponding to said physiological parameter and said selectively optimized adjustment parameter for one or more segments of said mammalian system.

86. (Original) The computer system of claim 83, wherein said physiologic pharmacokinetic simulation model comprises control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammalian system.

87. (Original) The computer system of claim 86, wherein said control statement rules are IF...THEN production rules.

88. (Original) The computer system of claim 83, wherein said input/output system comprises a user interface.

89. (Currently Amended) The computer system of claim 83, wherein said simulation ~~engine~~ model further comprises ~~a differential~~ an equation solver.

90. (Original) The computer system of claim 83, wherein said pharmacokinetic property is selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

91. (Original) The computer system of claim 83, wherein said absorption parameter is selected from the group consisting of concentration, permeability, solubility, dissolution rate, transport mechanism, and formulation release rate.

92. (Currently Amended) The ~~article of manufacture~~ computer system of claim 83, wherein said physiological parameter is selected from the group consisting of pH, fluid volume, fluid volume transfer rate, fluid absorption, surface area, and transit time.

93. (Original) The computer system of claim 83, wherein said mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

94. (Original) The computer system of claim 93, wherein said mammalian system of interest is gastrointestinal tract and said segments are selected from the group consisting of stomach, duodenum, jejunum, ileum and colon.

95. (Original) The computer system of claim 83, wherein said input data includes data selected from the group consisting of dissolution rate, transport mechanism and formulation release rate.

96. (Currently Amended) The computer system of claim 83, wherein said ~~differential~~ equations comprise one or more input variables corresponding to said input data for calculating as one or more output variables said change in said physiological parameter.

97. (Currently Amended) The computer system of claim 83, wherein said ~~differential~~ equations comprise one or more input variables corresponding to said input data for calculating as one or more output variables said change in said absorption parameter.

98. (Original) The computer system of claim 83, wherein said selectively optimized adjustment parameter correlates said input data to output data comprising said pharmacokinetic property of said compound.

99. (Currently Amended) The computer system of claim 98, wherein said input data comprises in vitro data and said selectively optimized adjustment parameter comprises a best fit value obtained by (i) assigning an initial value to a selected adjustment parameter of said simulation model, (ii) fitting a combination of in vitro data and in vivo data for different compounds of a compound test set with said simulation model, (iii)

selecting a best fit value for said selected adjustment parameter that, when assigned as an initial value to said selected adjustment parameter, permits said simulation model to predict said pharmacokinetic property of said compound when said input data comprises said in vitro data, and (iv) assigning said best fit value as a constant to said selected adjustment parameter so as to generate said selectively optimized adjustment parameter that modifies one or more of said ~~differential~~ equations.

100. (Original) The computer system of claim 99, wherein said in vitro data is obtained from testing of a compound in one or more assays that generate data selected from the group consisting of cell, tissue, structure-activity relationship (SAR), and quantitative structure-activity relationship (QSAR) data.

101. (Original) The computer system of claim 99, wherein said different compounds of a compound test set comprise compounds having diverse pharmacokinetic properties in said mammalian system of interest.

102. (Currently Amended) The computer system of claim 98, wherein said input data comprises in vivo data from a first species of mammal and said mammalian system of interest comprises a second species of mammal, and wherein said selectively optimized adjustment parameter comprises a best fit value obtained by (i) assigning an initial value to a selected adjustment parameter of said simulation model, (ii) fitting a combination of in vivo data with said simulation model, said combination of in vivo data derived from testing of different compounds of a compound test set in said first species of mammal and said second species of mammal, (iii) selecting a best fit value for said selected adjustment parameter that, when assigned as an initial value to said selected

adjustment parameter, permits said simulation model to predict said pharmacokinetic property of said compound when said input data comprises said in vitro data from said first species of mammal, and (iv) assigning said best fit value as a constant to said selected adjustment parameter so as to generate said selectively optimized adjustment parameter that modifies one or more of said ~~differential~~ equations.

103. (Original) The computer system of claim 102, wherein said different compounds of a compound test set comprise compounds having diverse pharmacokinetic properties in said mammalian system of interest.

104. (Original) The computer system of claim 83, wherein said selectively optimized adjustment parameter is for one or more of fluid absorption, flux, permeability, transport mechanism, transfer rate, and segment surface area.

105. (Original) The computer system of claim 103, wherein said physiologic pharmacokinetic simulation model comprises at least two of said anatomical segments and a logic function module comprising a regional correlation estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property of said compound in a first anatomical segment when supplied with an input value corresponding to said selected pharmacokinetic property in a second anatomical segment and with a regional correlation coefficient for said selected pharmacokinetic property of said first and second anatomical segments.

106. (Currently Amended) A computer system for simulating a pharmacokinetic property of a compound in a mammal of interest utilizing regional correlation parameter

estimation, said computer system comprising as operably linked computer-implemented components an input/output system~~, a simulation engine,~~ and a physiologic pharmacokinetic simulation model of at least two segments of a selected mammalian system of interest, said physiologic pharmacokinetic simulation model comprising (i) ~~differential~~ equations for calculating the change in one or more physiological parameters of first and second segments of said mammalian system of interest and the movement and disposition of said compound in said first and second segments as a function of time, and (ii) a logic function module having a regional correlation parameter estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property ~~comprising an absorption parameter~~ of said compound in said first segment when supplied with an input value corresponding to said selected pharmacokinetic property of said compound in said second segment and with a regional correlation coefficient for said selected pharmacokinetic parameter of said first and second segments;

said input/output system~~, said simulation engine,~~ and said physiologic pharmacokinetic simulation model being capable of working together to carry out the steps of:

(a) receiving through said input/output system input data comprising a pharmacokinetic property of said compound in said second segment of said mammalian system of interest; and

(b) applying ~~said simulation engine and~~ said physiologic pharmacokinetic simulation model to initiate said estimation function to estimate said pharmacokinetic property of said compound in said first segment of said mammalian system of interest,

wherein the regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the regional correlation coefficient;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient with the new value selected in step (iv).

107. (Original) The computer system of claim 106, wherein said regional correlation estimation function comprises a function/transformation algorithm.

108. (Original) The computer system of claim 107, wherein said function/transformation algorithm is selected from the group consisting of a polynomial, exponential, and logarithm.

109. (Original) The computer system of claim 106, wherein said regional correlation coefficient comprises a best fit value that transforms said input data

comprising said pharmacokinetic property of said compound in said second segment to an estimated pharmacokinetic property of said compound in said first segment.

110. (Original) The computer system of claim 106, wherein said pharmacokinetic property is selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

111. (Original) The computer system of claim 106, wherein said pharmacokinetic parameter is selected from the group consisting of permeability, solubility, dissolution rate and transport mechanism.

112. (Currently Amended) The computer system of claim 106, wherein said ~~differential~~ equations are selected from the group consisting of equations for fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption.

113. (Original) The computer system of claim 106, wherein said mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

114. (Original) The computer system of claim 83 or 106, wherein said mammalian system of interest is human.

115. (Original) The computer system of claim 106, wherein said input data comprises in vitro data.

116. (Original) The computer system of claim 115, wherein said in vitro data is derived from testing of said compound in an assay that generates data selected from

the group consisting of cell, tissue, physicochemical, structure-activity relationship (SAR) SAR, and quantitative structure-activity relationship (QSAR) QSAR data.

117. (Original) The computer system of claim 106, wherein said computer system comprises a data processor, a memory and a display.

118. (Original) The computer system of claim 106, wherein said input/output system comprises a user interface.

119. (Currently Amended) The computer system of claim 106, wherein said ~~simulation engine~~ computer system further comprises ~~a differential~~ an equation solver.

120. (Original) The computer system of claim 106, wherein said physiologic pharmacokinetic simulation model comprises a subsystem of said computer system.

121. (Currently Amended) The computer system of claim 106, wherein one or more of said ~~differential~~ equations is modified by a selectively optimized adjustment parameter.

122-136. Cancel.

137. (Currently Amended) An article of manufacture comprising a computer readable medium having computer readable program code embodied therein for simulating absorption of a target compound in a mammal of interest, and having

~~(a) computer readable simulation engine program code, and~~

~~(b)~~ computer readable simulation model code of one or more segments of a selected mammalian system having one or more physiological barriers to absorption of

said target compound, said computer readable simulation model comprising as operably linked components:

(i) differential equations for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system, and

(ii) control statement rules for one or more segments of said mammalian system;

said computer readable ~~simulation engine code and~~ simulation model code being ~~being~~ configured to carry out the steps of:

(a) receiving input data for a compound for one or more segments of a data source system; and

(b) applying ~~said computer readable simulation engine code and~~ said computer readable simulation model code to simulate absorption of said target compound relative to one or more segments of said target mammalian system,

wherein the simulation model comprises a selected adjustment parameter and wherein the selected adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selected adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selected adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selected adjustment parameter in the simulation model with the new value selected in step (iv).

138. (Currently Amended) An article of manufacture comprising a computer readable medium having computer readable program code embodied therein for simulating absorption of a compound in a mammal of interest, and having computer readable input/output system~~, computer readable simulation engine,~~ and computer readable simulation model of one or more segments of a selected mammalian system having one or more physiological barriers to absorption of said compound based on a selected route of administration, said computer readable simulation model comprising as operably linked components:

(i) ~~differential~~ equations for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system and; (ii) initial parameter values for said ~~differential~~ equations corresponding to physiological parameters and a selectively optimized adjustment ~~parameters~~ parameter~~, and optionally one or more regional correlation parameters, for one or more segments of said mammalian system; and optionally (iii) control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammalian system~~;

said computer readable input/output system~~, said computer readable simulation engine,~~ and said computer readable simulation model being capable of working together to carry out the steps of:

(a) receiving as input data through said computer readable input/output system, dose, permeability and solubility data for said compound for one or more segments of said mammalian system; and

(b) applying ~~said computer readable simulation engine and~~ said computer readable simulation model to simulate absorption of said compound relative to one or more segments of said mammalian system of interest,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively optimized adjustment parameter in the simulation model with the new value selected in step (iv).

139. (Original) The article of manufacture of claim138, wherein said mammalian system is selected from the group consisting of the gastrointestinal tract, the eye, the nose, the lung, the skin, and the brain.

140. (Original) The article of manufacture of claim 139, wherein said mammalian system is the gastrointestinal tract.

141. (Original) The article of manufacture of claim 140, wherein said segments are selected from the group consisting of stomach, duodenum, jejunum, ileum, and colon.

142. (Original) The article of manufacture of claim 138, wherein said simulation model corresponds to a compartment-flow model comprising compartments that are operably linked through flow regulators modified by one or more converters.

143. (Original) The article of manufacture of claim 142, wherein said compartments comprise one or more compartments characterized by a parameter selected from the group consisting of fluid volume, fluid absorption, formulation, insoluble mass, soluble mass, and soluble mass absorption.

144. (Original) The article of manufacture of claim 142, wherein said flow regulators are characterized by a parameter selected from the group consisting of fluid absorption rate, fluid transit rate, formulation transit rate, formulation release rate, insoluble mass transit rate, insoluble mass dissolution rate, soluble mass transit rate, and soluble mass absorption rate.

145. (Original) The article of manufacture of claim 142, wherein said converters are characterized by a parameter selected from the group consisting of fluid volume,

fluid volume absorption rate constant, fluid volume transit rate constant, insoluble mass, insoluble mass transit rate constant, dissolution rate constant, soluble mass, soluble mass transit rate constant, surface area, dissolved mass concentration and permeability.

146. (Currently Amended) The article of manufacture of claim 142, wherein one or more of said converters are characterized by ~~a~~ the selectively optimized adjustment parameter.

147. (Original) The article of manufacture of claim 142, wherein one or more of said converters are characterized by a regional correlation parameter.

148. (Original) The article of manufacture of claim 138, wherein said control statement rules are IF...THEN production rules.

149. (Original) The article of manufacture of claim 138, wherein said physiological parameters are characterized by a parameter selected from the group consisting of soluble mass transfer rate constant, permeability, solubility, dissolution rate, and transport mechanism.

150. (Original) The article of manufacture of claim 138, wherein said physiological parameters are characterized by a parameter selected from the group consisting of pH, initial fluid volume, surface area, fluid volume transit time, insoluble mass transit time, soluble mass transit time, fluid volume transfer rate, and fluid absorption rate.

151. (Original) The article of manufacture of claim 138, wherein said mammal is human.

152. (Original) The article of manufacture of claim 138, where said input data further comprises data for said compound of interest selected from the group consisting of dissolution rate, transport mechanism, transit time, pH and formulation release rate.

153. (Original) The article of manufacture of claim 138, wherein said input data is in vitro data.

154. (Original) The article of manufacture of claim 153, wherein said in vitro data is permeability data derived from an assay selected from the group consisting of a cell-based assay and a tissue-based assay.

155. (Original) The article of manufacture of claim 153, wherein said in vitro data is transport mechanism data derived from an assay selected from the group consisting of a cell-based assay and a tissue-based assay.

156. (Original) The article of manufacture of claim 153, wherein said in vitro data is permeability data derived from structure-activity relationship data of said compound.

157. (Original) The article of manufacture of claim 153, wherein said in vitro data is dissolution rate data derived from structure-activity relationship data of said compound.

158. (Original) The article of manufacture of claim 153, wherein said in vitro data is solubility data derived from structure-activity relationship data of said compound.

159. (Currently Amended) A computer program product for simulating absorption of a compound in a mammal, and having computer readable program code input/output

system~~, computer readable program code simulation engine,~~ and computer readable program code simulation model of one or more segments of a selected mammalian system having one or more physiological barriers to absorption based on a selected route of administration, said computer readable program code simulation model comprising as operably linked components:

(i) ~~differential~~ equations for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system; (ii) initial parameter values for said differential equations corresponding to physiological parameters and a selectively optimized adjustment parameter ~~parameters, and optionally regional correlation parameters, for one or more segments of said mammalian system~~; and (iii) control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammalian system;

wherein said computer readable program code input/output system~~, said computer readable program code simulation engine,~~ and said computer readable program code simulation model being capable of working together to carry out the steps of:

(a) receiving as input data through said computer readable program code input/output system, dose, permeability and solubility data for said compound for one or more segments of said mammalian system; and

(b) applying ~~said computer readable program code simulation engine and~~ said computer readable program code simulation model to simulate absorption of said compound relative to one or more segments of said mammalian system,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively optimized adjustment parameter in the simulation model with the new value selected in step (iv).

160. (Currently Amended) An article of manufacture comprising a computer readable medium having computer readable program code embodied therein for simulating a pharmacokinetic property of a compound in a mammal of interest, and having computer readable input/output system, computer readable simulation engine, and computer readable physiologic pharmacokinetic simulation model of one or more anatomical segments of a selected mammalian system, said computer readable physiologic pharmacokinetic simulation model comprising ~~differential~~ equations for calculating as a function of time the change in (i) a physiological parameter of one or more of said segments and (ii) a pharmacokinetic property ~~comprising an absorption parameter~~ of a compound relative to a selected route of administration~~, barrier to absorption~~ and sampling site of one or more of said segments, wherein one or more of said ~~differential~~ equations is modified by a selectively optimized adjustment parameter;

said computer readable input/output system, said computer readable simulation engine, and said computer readable physiologic pharmacokinetic simulation model being capable of working together to carry out the steps of:

(a) receiving through said computer readable input/output system input data comprising ~~dose, permeability and solubility~~ pharmacokinetic data for said compound for one or more segments of said mammalian system of interest; and

(b) applying said computer readable simulation engine and said computer readable physiologic pharmacokinetic simulation model to simulate a pharmacokinetic property of said compound relative to one or more segments of said mammalian system of interest,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively otimized adjustment parameter in the simulation model with the new value selected in step (iv).

161. (Currently Amended) The article of manufacture of claim 160, wherein said ~~differential~~ equations are for one or more of fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption for one or more segments of said mammalian system.

162. (Currently Amended) The article of manufacture of claim 160, wherein said ~~differential~~ equations comprise initial parameter values corresponding to said physiological parameter and said selectively optimized adjustment parameter for one or more segments of said mammalian system.

163. (Original) The article of manufacture of claim 160, wherein said physiologic pharmacokinetic simulation model comprises control statement rules for one or more of transit, absorption, permeability, solubility, dissolution, and concentration for one or more segments of said mammalian system.

164. (Original) The article of manufacture of claim 163, wherein said control statement rules are IF...THEN production rules.

165. (Original) The article of manufacture of claim 160, wherein said input/output system comprises a user interface.

166. (Currently Amended) The article of manufacture of claim 160, wherein said simulation engine comprises an~~a differential~~ equation solver.

167. (Currently Amended) The article of manufacture of claim 160, wherein said ~~absorption~~ physiological parameter is selected from the group consisting of

concentration, permeability, solubility, dissolution rate, transport mechanism, and formulation release rate.

168. (Original) The article of manufacture of claim 160, wherein said physiological parameter is selected from the group consisting of pH, fluid volume, fluid volume transfer rate, fluid absorption, surface area, and transit time.

169. (Original) The article of manufacture of claim 160, wherein said mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

170. (Original) The article of manufacture of claim 169, wherein said mammalian system of interest is gastrointestinal tract and said segments are selected from the group consisting of stomach, duodenum, jejunum, ileum and colon.

171. (Original) The article of manufacture of claim 160, wherein said input data includes data selected from the group consisting of dissolution rate, transport mechanism and formulation release rate.

172. (Currently Amended) The article of manufacture of claim 160, wherein said ~~differential~~ equations comprise one or more input variables corresponding to said input data for calculating as one or more output variables said change in said physiological parameter.

173. (Currently Amended) The article of manufacture of claim 160, wherein said ~~differential~~ equations comprise one or more input variables corresponding to said input

data for calculating as one or more output variables said change in said absorption parameter.

174. (Original) The article of manufacture of claim 160, wherein said selectively optimized adjustment parameter correlates said input data to output data comprising said pharmacokinetic property of said compound.

175. (Currently Amended) The article of manufacture of claim 174, wherein said input data comprises in vitro data and said selectively optimized adjustment parameter comprises a best fit value obtained by (i) assigning an initial value to a selected adjustment parameter of said simulation model, (ii) fitting a combination of in vitro data and in vivo data for different compounds of a compound test set with said simulation model, (iii) selecting a best fit value for said selected adjustment parameter that, when assigned as an initial value to said selected adjustment parameter, permits said simulation model to predict said pharmacokinetic property of said compound when said input data comprises said in vitro data, and (iv) assigning said best fit value as a constant to said selected adjustment parameter so as to generate said selectively optimized adjustment parameter that modifies one or more of said ~~differential~~ equations.

176. (Original) The article of manufacture of claim 175, wherein said in vitro data is obtained from testing of a compound in one or more assays that generate data selected from the group consisting of cell, tissue, structure-activity relationship (SAR), and quantitative structure-activity relationship (QSAR) data.

177. (Original) The article of manufacture of claim 175, wherein said different compounds of a compound test set comprise compounds having diverse pharmacokinetic properties in said mammalian system of interest.

178. (Currently Amended) The article of manufacture of claim 174, wherein said input data comprises in vivo data from a first species of mammal and said mammalian system of interest comprises a second species of mammal, and wherein said selectively optimized adjustment parameter comprises a best fit value obtained by (i) assigning an initial value to a selected adjustment parameter of said simulation model, (ii) fitting a combination of in vivo data with said simulation model, said combination of in vivo data derived from testing of different compounds of a compound test set in said first species of mammal and said second species of mammal, (iii) selecting a best fit value for said selected adjustment parameter that, when assigned as an initial value to said selected adjustment parameter, permits said simulation model to predict said pharmacokinetic property of said compound when said input data comprises said in vitro data from said first species of mammal, and (iv) assigning said best fit value as a constant to said selected adjustment parameter so as to generate said selectively optimized adjustment parameter that modifies one or more of said ~~differential~~ equations.

179. (Original) The article of manufacture of claim 178, wherein said different compounds of a compound test set comprise compounds having diverse pharmacokinetic properties in said mammalian system of interest.

180. (Original) The article of manufacture of claim 160, wherein said selectively optimized adjustment parameter is for one or more of fluid absorption, flux, permeability, transport mechanism, transfer rate, and segment surface area.

181. (Original) The article of manufacture of claim 160, wherein said computer readable physiologic pharmacokinetic simulation model comprises at least two of said anatomical segments and a logic function module comprising a regional correlation estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property of said compound in a first anatomical segment when supplied with an input value corresponding to said selected pharmacokinetic property in a second anatomical segment and with a regional correlation coefficient for said selected pharmacokinetic property of said first and second anatomical segments.

182. (Currently Amended) A computer program product for simulating a pharmacokinetic property of a compound in a mammal of interest, and having computer readable program code input/output system, computer readable program code simulation engine, and computer readable program code physiologic pharmacokinetic simulation model of one or more anatomical segments of a selected mammalian system, said computer readable program code physiologic pharmacokinetic simulation model comprising ~~differential~~ equations for calculating as a function of time the change in (i) a physiological parameter of one or more of said segments and (ii) a pharmacokinetic property ~~comprising an absorption parameter~~ of a compound ~~relative to a selected route of administration, barrier to absorption and sampling site of one or~~

~~more of said segments~~, wherein one or more of said ~~differential~~ equations ~~is~~ are modified by a selectively optimized adjustment parameter;

said computer readable program code input/output system, said computer readable program code simulation engine, and said computer readable program code physiologic pharmacokinetic simulation model being capable of working together to carry out the steps of:

(a) receiving through said computer readable program code input/output system input data comprising dose, permeability and solubility data for said compound for one or more segments of said mammalian system of interest; and

(b) applying said computer readable program code simulation engine and said computer readable program code physiologic pharmacokinetic simulation model to simulate a pharmacokinetic property ~~comprising an absorption parameter~~ of said compound relative to one or more segments of said mammalian system of interest,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively optimized adjustment parameter in the simulation model with the new value selected in step (iv).

183. (Original) The article of manufacture of claim 182, wherein said computer readable program code physiologic pharmacokinetic simulation model comprises at least two of said anatomical segments and a logic function model comprising a regional correlation estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property of said compound in a first anatomical segment when supplied with an input value corresponding to said selected pharmacokinetic property in a second anatomical segment and with a regional correlation coefficient for said selected pharmacokinetic property of said first and second anatomical segments.

184. (Currently Amended) An article of manufacture comprising a computer readable medium having computer readable program code embodied therein for simulating a pharmacokinetic property of a compound in a mammal of interest, and having computer readable input/output system, computer readable simulation engine, and computer readable physiologic pharmacokinetic simulation model of at least two segments of a selected mammalian system of interest, said computer readable physiologic pharmacokinetic simulation model comprising as operably linked components:

(i) ~~differential~~ equations for calculating the change in one or more physiological parameters of first and second segments of said mammalian system of interest and the movement and disposition of said compound in said first and second segments as a

function of time, and (ii) a logic function module having a regional correlation parameter estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property ~~comprising an absorption parameter~~ of said compound in said first segment when supplied with an input value corresponding to said selected pharmacokinetic property of said compound in said second segment and with a regional correlation coefficient for said selected pharmacokinetic parameter of said first and second segments;

said computer readable input/output system, said computer readable simulation engine, and said computer readable physiologic pharmacokinetic simulation model being capable of working together to carry out the steps of:

(a) receiving through said computer readable input/output system input data comprising a pharmacokinetic property of said compound in said second segment of said mammalian system of interest; and

(b) applying said computer readable simulation engine and said computer readable physiologic pharmacokinetic simulation model to initiate said estimation function to estimate said pharmacokinetic property of said compound in said first segment of said mammalian system of interest,

wherein the regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the at least one regional correlation coefficient;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of

the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient in the model with the new value selected in step (iv).

185. (Original) The article of manufacture of claim 184, wherein said regional correlation estimation function comprises a function/transformation algorithm.

186. (Original) The article of manufacture of claim 185, wherein said function/transformation algorithm is selected from the group consisting of a polynomial, exponential, and logarithm.

187. (Original) The article of manufacture of claim 184, wherein said regional correlation coefficient comprises a best fit value that transforms said input data comprising said pharmacokinetic property of said compound in said second segment to an estimated pharmacokinetic property of said compound in said first segment.

188. (Original) The article of manufacture of claim 160 or 184, wherein said pharmacokinetic property is selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

189. (Original) The article of manufacture of claim 184, wherein said pharmacokinetic parameter is selected from the group consisting of permeability, solubility, dissolution rate and transport mechanism.

190. (Currently Amended) The article of manufacture of claim 184, wherein said ~~differential~~ equations are selected from the group consisting of equations for fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption.

191. (Original) The article of manufacture of claim 184, wherein said mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

192. (Original) The article of manufacture of claim 160 or 184, wherein said mammalian system of interest is human.

193. (Original) The article of manufacture of claim 184, wherein said input data comprises in vitro data.

194. (Original) The article of manufacture of claim 193, wherein said in vitro data is derived from testing of said compound in an assay that generates data selected from the group consisting of cell, tissue, physicochemical, structure-activity relationship (SAR) SAR, and quantitative structure-activity relationship (QSAR) QSAR data.

195. (Currently Amended) The article of manufacture of claim 184, wherein one or more of said ~~differential~~ equations is modified by a selectively optimized adjustment parameter.

196. (Currently Amended) A computer program product for simulating a pharmacokinetic property of a compound in a mammal of interest, and having computer readable program code input/output system~~, computer readable program code simulation engine,~~ and computer readable program code physiologic pharmacokinetic simulation model of at least two segments of a selected mammalian system of interest, said computer readable program code physiologic pharmacokinetic simulation model comprising as operably linked components:

(i) ~~differential equations~~ calculating means for calculating the change in one or more physiological parameters of first and second segments of said mammalian system of interest and the movement and disposition of said compound in said first and second segments as a function of time, and (ii) a logic function module having a regional correlation parameter estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property comprising an absorption parameter of said compound in said first segment when supplied with an input value corresponding to said selected pharmacokinetic property of said compound in said second segment and with a regional correlation coefficient for said selected pharmacokinetic parameter of said first and second segments;

said computer readable program code input/output system~~, said computer readable program code simulation engine,~~ and said computer readable program code physiologic pharmacokinetic simulation model being capable of working together to carry out the steps of:

(a) receiving through said computer readable program code input/output system input data comprising a pharmacokinetic property of said compound in said second segment of said mammalian system of interest; and

(b) applying ~~said computer readable program code simulation engine and~~ said computer readable program code physiologic pharmacokinetic simulation model to initiate said estimation function to estimate said pharmacokinetic property of said compound in said first segment of said mammalian system of interest,

wherein the at least one regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the regional correlation coefficient of the simulation model;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient in the simulation model with the new value selected in step (iv).

197. (Currently Amended) The computer program product of claim 196, wherein one or more of said ~~differential equations~~ calculating means is modified by ~~a~~ the selectively optimized adjustment parameter.

198. (Currently Amended) An article of manufacture comprising a computer readable medium having embodied therein a computer readable physiologic pharmacokinetic simulation model of one or more anatomical segments of a selected mammalian system, said computer readable physiologic pharmacokinetic simulation model comprising calculating means ~~differential equations~~ for calculating as a function of time the change in (i) a physiological parameter of one or more of said segments and (ii) a pharmacokinetic property comprising an absorption parameter of a compound relative to a selected route of administration, barrier to absorption and sampling site of one or more of said segments, wherein one or more of said calculating means ~~differential equations~~ is modified by a selectively optimized adjustment parameter,

wherein the selectively optimized adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selectively optimized adjustment parameter;

(ii) inputting first data for a plurality of compounds into the simulation model and running the model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selectively optimized adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selectively optimized adjustment parameter in the simulation model with the new value selected in step (iv).

199. (Currently Amended) An article of manufacture comprising a computer readable medium having embodied therein a computer readable physiologic pharmacokinetic simulation model of at least two segments of a selected mammalian system of interest, said computer readable physiologic pharmacokinetic simulation model comprising as operably linked components:

(i) ~~differential~~ equations for calculating the change in one or more physiological parameters of first and second segments of said mammalian system of interest and the movement and disposition of said compound in said first and second segments as a function of time, and (ii) a logic function module having a regional correlation parameter estimation function and a control statement for initiating said function, wherein said estimation function when initiated is capable of generating an estimated value for a selected pharmacokinetic property comprising an absorption parameter of said compound in said first segment when supplied with an input value corresponding to said selected pharmacokinetic property of said compound in said second segment and with a regional correlation coefficient for said selected pharmacokinetic parameter of said first and second segments,

wherein the at least one regional correlation coefficient comprises a value obtained by:

(i) assigning an initial value to the regional correlation coefficient of the simulation model;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the simulation model and running the simulation model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the regional correlation coefficient such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the regional correlation coefficient in the simulation model with the new value selected in step (iv).

200. (New) A method of predicting a pharmacokinetic property of a compound in a first anatomical segment of a mammalian system from a pharmacokinetic property of the compound in a second anatomical segment of the mammalian system, the method comprising:

providing a model, the model predicting the change in one or more physiological parameters of the first and second anatomical segments and the movement and disposition of the compound in the first and second segments as a function of time, the model comprising at least one regional correlation parameter, wherein the at least one regional correlation parameter comprises a value obtained by:

(i) assigning an initial value to the at least one regional correlation parameter of the model;

(ii) inputting first data for a plurality of compounds in the second anatomical segment of the mammalian system into the model and running the model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds in the first anatomical segment of a mammalian system;

(iv) selecting a new value for the at least one regional correlation parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value for the at least one regional correlation parameter in the model with the new value selected in step (iv); and

using the model to predict the pharmacokinetic property of the compound in the first anatomical segment of the mammalian system from the pharmacokinetic property of the compound in the second anatomical segment of the mammalian system.

201. (New) The method of claim 200, wherein the value is further obtained by repeating steps (ii)-(v) one or more times until a difference between the output data and the second data source is less than the largest of the experimental error in the first or second data for a particular compound in the plurality of compounds or the inter-day variation in the first or second data for a particular compound in the plurality of compounds.

202. (New) The method of claim 201, wherein the difference is determined by one of the following: normalized difference, collective regression coefficient, normalized arithmetic mean, normalized median, normalized geometric mean, normalized harmonic mean, variance, standard deviation, and coefficient of variation.

203. (New) The method of claim 200, wherein the model determines a change in one or more physiological parameters of the first and second segments and movement and disposition of the compound in the first and second segments as a function of time.

204. (New) The method of claim 203, wherein the model further comprises a regional correlation estimation algorithm.

205. (New) The method of claim 204, wherein the algorithm is selected from the group consisting of a polynomial, exponential, and logarithm.

206. (New) The method of claim 204, wherein the algorithm is selected from the group consisting of equations for fluid transit, fluid absorption, mass transit, mass dissolution, mass solubility, and mass absorption.

207. (New) The method of claim 200, wherein the pharmacokinetic property is selected from the group consisting of absorption, distribution, metabolism, elimination and toxicity.

208. (New) The method of claim 200, wherein the pharmacokinetic property is selected from the group consisting of permeability, solubility, dissolution rate and transport mechanism.

209. (New) The method of claim 200, further comprising:

reversibly storing the estimated value for the pharmacokinetic parameter of the compound in the first segment in a database.

210. (New) The method of claim 200, further comprising:

reversibly storing in a computer-implemented database an output value generated by the model corresponding to the pharmacokinetic property of the compound in a segment of the mammalian system.

211. (New) The method of claim 200, wherein the mammalian system is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

212. (New) The method of claim 200, wherein the first data comprises in vitro data.

213. (New) The method of claim 212, wherein the in vitro data is derived from testing of the compound in an assay that generates data selected from the group consisting of cell, tissue, physicochemical, structure-activity relationship (SAR) SAR, and quantitative structure-activity relationship (QSAR) QSAR data.

214. (New) The method of claim 200, wherein the model is provided on a computer system having a data processor, a memory and a display.

215. (New) The method of claim 200, wherein the at least one regional correlation parameter is a plurality of regional correlation parameters, and wherein step (i) assigns an initial value to each of the plurality of regional correlation parameters, step (iv) selects a new value for one or more of the plurality of regional correlation parameters, and step (v) replaces the value of the one or more of the plurality of regional correlation parameters with the new value selected in step (iv).

216. (New) A method for predicting a pharmacokinetic property of a compound in a mammalian system of interest, the method comprising:

providing a model, the model predicting the change in one or more physiological parameters and the movement and disposition of the compound in the mammalian system of interest as a function of time, wherein the model comprises a selected adjustment parameter and wherein the selected adjustment parameter comprises a value obtained by:

(i) assigning an initial value to the selected adjustment parameter;

(ii) inputting first data for a plurality of compounds into the model and running the model to generate output data;

(iii) comparing the output data with second data for the plurality of compounds;

(iv) selecting a new value for the selected adjustment parameter such that deviation of the comparison in step (iii) is reduced; and

(v) replacing the value of the selected adjustment parameter in the model with the new value selected in step (iv);

using the model to predict a pharmacokinetic property of a particular compound.

217. (New) The method of claim 216, further comprising:

(vi) repeating steps (ii)-(v) one or more times until a difference between the output data and the second data is less than the largest experimental error in the first or second data or less than the largest interday variation in the first or second data.

218. (New) The method of claim 217, wherein the difference is determined by one of the following: normalized difference, collective regression coefficient, normalized arithmetic mean, normalized median, normalized geometric mean, normalized harmonic mean, variance, standard deviation, or coefficient of variation.

219. (New) The method of claim 216, wherein the selected adjustment parameter is a plurality of selected adjustment parameters and wherein step (i) assigns an initial value to each of the plurality of selected adjustment parameters, step (iv) selects a new value for one or more of the plurality of selected adjustment parameters, and step (v) replaces the value for the one or more of the plurality of selected adjustment parameters with the new value selected in step (iv).

220. (New) The method of claim 216, wherein the selected adjustment parameter value is selected from the group consisting of a constant, a range of constants, a function and an algorithm.

221. (New) The method of claim 216, wherein the model comprises a physiologic pharmacokinetic model of one or more anatomical segments of the mammalian system of interest.

222. (New) The method of claim 221, wherein the physiologic pharmacokinetic model determines the change in one or more physiological parameters of the one or more anatomical segments and the movement and disposition of the compound in the one or more anatomical segments as a function of time.

223. (New) The method of claim 221, wherein the mammalian system of interest is selected from the group consisting of gastrointestinal tract, liver, heart, kidney, eye, nose, lung, skin and brain.

224. (New) The method of claim 221, wherein the first data corresponds to one or more in vitro properties for each of the plurality of compounds.

225. (New) The method of claim 224, wherein the first data is derived from testing of each of the plurality of compounds for at least one in vitro property in an assay that generates data, the assay selected from the group consisting of cell, tissue, physicochemical, structure-activity relationship (SAR), and quantitative structure-activity relationship (QSAR).

226. (New) The method of claim 224, wherein the in vitro properties are selected from the group consisting of absorption, distribution, metabolism, elimination, and toxicity.

227. (New) The method of claim 221, wherein the second data corresponds to one or more in vivo properties for each of the plurality of compounds.

228. (New) The method of claim 227, wherein the in vivo properties are selected from the group consisting of absorption, distribution, metabolism, elimination, and toxicity.

229. (New) The method of claim 227, wherein the plurality of compounds include compounds exhibiting different in vivo properties in the mammalian system of interest.

230. (New) The method of claim 229, wherein the in vivo properties are selected from the group consisting of permeability, solubility, dissolution, activity, metabolism, and toxicity.

231. (New) The method of claim 230, wherein the one or more in vivo properties are derived from testing each of the plurality of compounds in the mammalian system of interest.